This patent application includes a computer program listing appendix (Appendix), which contains the source code for the software used in carrying out the examples in accordance with the present invention. The Appendix is contained on one compact disc submitted in duplicate and designated as Copy 1 and Copy 2. The Appendix is in a single file that is 292 kB in size and designated "computer program listing appendix U.S. Serial No. 09-021,721". The file was created on 02/02/1998 and is a Microsoft Word document. The material in the Appendix is incorporated herein by reference.

A1

Please replace the paragraphs beginning on page 46, line 4, to page 50, line 35 with the following paragraphs (for the convenience of the Examiner, Applicant is also including a clean copy of pages 46-50, which may be substituted for the existing pages):

GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

Sequence	T_m (°C)	ΔG_{MFOLD}	
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CCAAAAAGGGTCAGTCTACCTCCCG	70.78	-1.20	SEQ ID NO: 12
CAAAAAGGGTCAGTCTACCTCCCGC	71.23	-1.20	SEQ ID NO: 13
AAAAAGGGTCAGTCTACCTCCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAGGGTCAGTCTACCTCCCGCCATA	79.03	-1.20	SEQ ID NO: 17
AGGGTCAGTCTACCTCCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCAGTCTACCTCCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCCGCCATAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCCGCCATAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCCGCCATAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCCGCCATAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTTC	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCGCCATAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CGCCATAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35

A2

Next, the oligonucleotide sequences are filtered on the basis of T_m. A high and low cut-off value may be selected, for example, $60°C \leq T_m \leq 85°C$. Thus, oligonucleotides having T_m values falling within the above range are retained. Those outside the range are

discarded, which is indicated below by lining out of those oligonucleotides and parameter
values.

GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

Sequence	T_m (°C)	ΔG_{MFOLD}	SEQ ID
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CCAAAAAGGGTCAGTCTACCTCCCG	70.78	-1.20	SEQ ID NO: 12
CAAAAAGGGTCAGTCTACCTCCCGC	71.23	-1.20	SEQ ID NO: 13
AAAAAGGGTCAGTCTACCTCCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAGGGTCAGTCTACCTCCCGCCATA	79.03	-1.20	SEQ ID NO: 17
AGGGTCAGTCTACCTCCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCAGTCTACCTCCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCCGCCATAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCCGCCATAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCCGCCATAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCCGCCATAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTTC	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
~~CCGCCATAAAAAACTCATGTTCAAG~~	~~57.98~~	-0.10	SEQ ID NO: 34
~~CGCCATAAAAAACTCATGTTCAAGA~~	~~56.20~~	-0.10	SEQ ID NO: 35

A2
cont

Next, the oligonucleotide sequences remaining after the above exercise are filtered on the basis of ΔG_{MFOLD} and are retained if the value is greater than - 0.4. Those oligonucleotides with a ΔG_{MFOLD} less than - 0.4 are discarded, which is indicated below by double lining out of those oligonucleotides and parameter values.

GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

	T_m (°C)	ΔG_{MFOLD}	
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CCAAAAAGGGTCAGTCTACCTCCCG	70.78	-1.20	SEQ ID NO: 12
CAAAAAGGGTCAGTCTACCTCCCGC	71.23	-1.20	SEQ ID NO: 13
AAAAAGGGTCAGTCTACCTCCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAGGGTCAGTCTACCTCCCGCCATA	79.03	-1.20	SEQ ID NO: 17
AGGGTCAGTCTACCTCCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCAGTCTACCTCCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCCGCCATAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCCGCCATAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCCGCCATAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCCGCCATAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTTC	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCGCCATAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CGCCATAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35

A2
cont

Clusters of retained oligonucleotides are identified and ranked based on cluster size. In this example a contiguous cluster of 13 retained oligonucleotides is identified by the vertical black bar on the left. All of the oligonucleotides in this cluster may be evaluated experimentally.

GTCCAAAAAGGGTCAGTCTACCTCCCGCCATAAAAAACTCATGTTCAAGA (target complement sequence) (SEQ ID NO: 9)

Sequence	T_m (°C)	ΔG_{MFOLD}	SEQ ID
GTCCAAAAAGGGTCAGTCTACCTCC	71.77	-1.20	SEQ ID NO: 10
TCCAAAAAGGGTCAGTCTACCTCCC	71.99	-1.20	SEQ ID NO: 11
CCAAAAAGGGTCAGTCTACCTCCCG	70.78	-1.20	SEQ ID NO: 12
CAAAAAGGGTCAGTCTACCTCCCGG	71.23	-1.20	SEQ ID NO: 13
AAAAAGGGTCAGTCTACCTCCCGCC	73.07	-1.20	SEQ ID NO: 14
AAAAGGGTCAGTCTACCTCCCGCCA	75.68	-1.20	SEQ ID NO: 15
AAAGGGTCAGTCTACCTCCCGCCAT	77.53	-1.20	SEQ ID NO: 16
AAGGGTCAGTCTACCTCCCGCCATA	79.03	-1.20	SEQ ID NO: 17
AGGGTCAGTCTACCTCCCGCCATAA	79.03	-1.20	SEQ ID NO: 18
GGGTCAGTCTACCTCCCGCCATAAA	76.85	-1.20	SEQ ID NO: 19
GGTCAGTCTACCTCCCGCCATAAAA	73.10	-0.80	SEQ ID NO: 20
GTCAGTCTACCTCCCGCCATAAAAA	69.50	0.90	SEQ ID NO: 21
TCAGTCTACCTCCCGCCATAAAAAA	65.60	0.90	SEQ ID NO: 22
CAGTCTACCTCCCGCCATAAAAAAC	64.96	0.90	SEQ ID NO: 23
AGTCTACCTCCCGCCATAAAAAACT	65.48	1.10	SEQ ID NO: 24
GTCTACCTCCCGCCATAAAAAACTC	66.36	2.40	SEQ ID NO: 25
TCTACCTCCCGCCATAAAAAACTCA	64.97	2.90	SEQ ID NO: 26
CTACCTCCCGCCATAAAAAACTCAT	63.96	2.70	SEQ ID NO: 27
TACCTCCCGCCATAAAAAACTCATG	62.58	1.10	SEQ ID NO: 28
ACCTCCCGCCATAAAAAACTCATGT	65.10	0.40	SEQ ID NO: 29
CCTCCCGCCATAAAAAACTCATGTT	64.96	0.10	SEQ ID NO: 30
CTCCCGCCATAAAAAACTCATGTTC	63.37	-0.10	SEQ ID NO: 31
TCCCGCCATAAAAAACTCATGTTCA	62.86	-0.10	SEQ ID NO: 32
CCCGCCATAAAAAACTCATGTTCAA	60.47	-0.10	SEQ ID NO: 33
CCGCCATAAAAAACTCATGTTCAAG	57.98	-0.10	SEQ ID NO: 34
CGCCATAAAAAACTCATGTTCAAGA	56.20	-0.10	SEQ ID NO: 35